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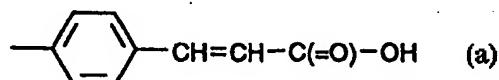
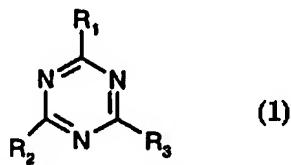
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(54) Title: SUNSCREEN COMPOSITIONS

(57) Abstract

The present invention provides a solution, suitable for use in pharmaceutical or cosmetic compositions, comprising a) 1-40 % by weight of a compound having formula (1), in which R₁, R₂ and R₃, independently, are H, OH, C₁-C₁₈alkoxy, NH₂, NH-R₄ or N(R₄)₂ in which R₄ is C₁-C₁₈alkyl, OR₄ in which R₄ has its previous significance, phenyl, phenoxy or anilino, or pyrrolo, in which the respective phenyl or pyrrolo moieties are optionally substituted by one, two or three substituents selected from OH, carboxy, C₁-C₁₈alkyl or -alkoxy, C₁-C₁₈carboxyalkyl, C₅-C₈cycloalkyl, a methylenecamphor group, a group -(CH=CH)_nC(=O)-OR₄ in which n is 0 or 1 and R₄ has its previous significance or a group (a) or the corresponding alkali metal, ammonium, mono-, di- or tri-C₁-C₄alkylammonium, mono-, di- or tri-C₂-C₄alkanolammonium salts, or the C₁-C₁₈alkyl esters thereof; dissolved in b) a solvent selected from i) a C₁-C₈alkyl ester of a (hydroxy)polycarboxylic acid, with the exclusion of dioctyl malate; ii) a butylether; iii) an ester of a butyl ether; iv) an alcohol; v) a Guerbet alcohol; and vi) a di-(C₁-C₄alkyl)amide of an arylcarboxylic acid.



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Sunscreen Compositions

The present invention relates to new formulations of UV absorbers and to their use in sunscreen compositions which, in turn, are useful, in particular, for the protection of human skin.

It has long been known that prolonged exposure to that UV radiation which reaches the surface of the earth can lead to the formation of erythemas or light dermatoses, as well as to an increased incidence of skin cancers or accelerated skin aging.

Various sunscreen formulations have been proposed which include a material which is intended to counteract UV radiation, thereby inhibiting the said undesired effects on the skin.

A great number of compounds has been proposed for use as UV protectants in sunscreen formulations, especially soluble organic UV absorbers and insoluble micronised inorganic compounds, in particular zinc oxide and titanium dioxide.

With respect to the use in sunscreen formulations of soluble organic UV absorbers, they have disadvantages that their effectiveness as UV protectants in terms of SPF (Sun Protection Factor) in a sunscreen formulation is often too low for commercial purposes; as a result of their solubility, they exhibit relatively high allergenic potential; and that, as a result of intrinsic photochemical lability, the duration of the protective effect is often too low.

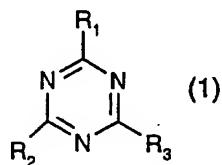
The high specific weight of insoluble inorganic compounds, such as zinc oxide and titanium dioxide leads to a reduced stability of formulations containing them. Moreover, such inorganic compounds have been claimed to generate toxic radicals under the influence of light ("Redox Mechanisms in Heterogeneous Photocatalysis", Serpone *et al*, Electrochemistry in Colloids and Dispersions, Editors Mackay and Texter, VCH Publishers Inc., New York 1992).

The preparation of small lipid nanoparticles for topical applications is known. For example, nanoparticles have been prepared by high pressure homogenisation using a microfluidizer.

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Lecithin was used as emulsifier and ethanol as co-surfactant, and the oil core contained a triglyceride and a relevant active ingredient, e.g. one of pharmaceutical or cosmetic interest.

One particular class of insoluble organic UV absorbers has now been found to provide particularly effective UV protection when used in sunscreen formulations. These UV absorbers are triazine compounds having the formula:



in which R₁, R₂ and R₃, independently, are H, OH, C₁-C₁₈alkoxy, NH₂, NH-R₄ or N(R₄)₂ in which R₄ is C₁-C₁₈alkyl, OR₄ in which R₄ has its previous significance, phenyl, phenoxy or anilino, or pyrrolo, in which the respective phenyl, phenoxy or anilino, or pyrrolo moieties are optionally substituted by one, two or three substituents selected from OH, carboxy, C₁-C₁₈alkyl or -alkoxy, C₁-C₁₈carboxyalkyl, C₅-C₈cycloalkyl, a methylenecamphor group, a group -(CH=CH)_nC(=O)-OR₄ in which n is 0 or 1 and R₄ has its previous significance, or

a group or the corresponding alkali metal,

ammonium, mono-, di- or tri-C₁-C₄alkylammonium, mono-, di- or tri-C₂-C₄alkanolammonium salts, or the C₁-C₁₈alkyl esters thereof.

In the compounds of formula (1), C₁-C₁₈alkyl groups may be methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, n-amyl, n-hexyl, n-heptyl, n-octyl, isoctyl, n-nonyl, n-decyl, n-undecyl, n-dodecyl, tetradecyl, hexadecyl or octadecyl.

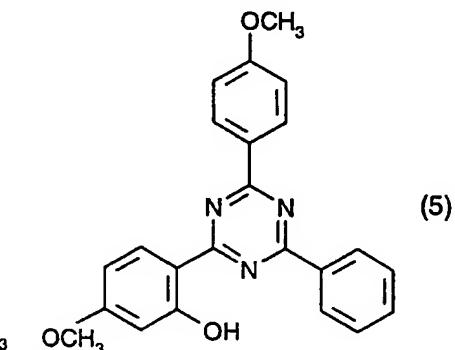
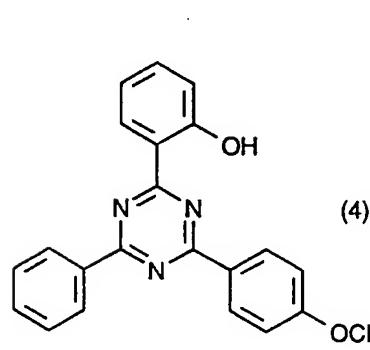
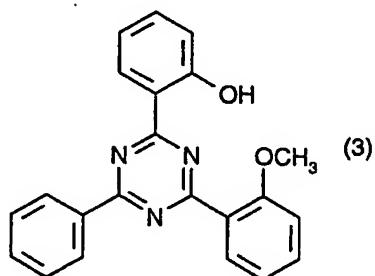
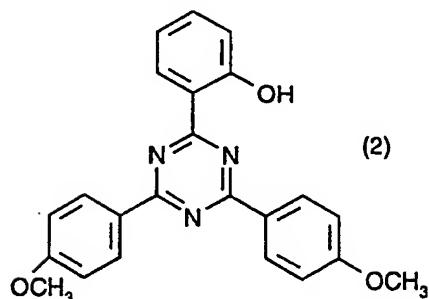
C₁-C₁₈alkoxy groups include methoxy, ethoxy, propoxy, butoxy, n-hexoxy, n-heptoxy, n-octoxy, isoctoxy, n-nonoxy, n-decoxy, n-undecoxy, n-dodecoxy, tetradecoxy, hexadecoxy or octadecoxy, methoxy and ethoxy being preferred.

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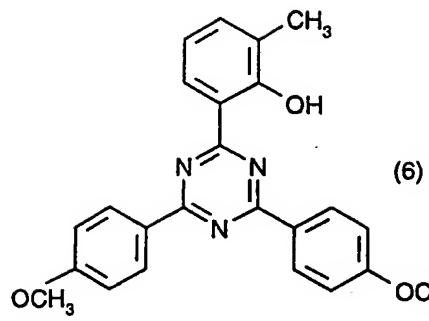
C₁-C₁₈carboxyalkyl includes carboxymethyl, carboxyethyl, carboxypropyl, carboxyisopropyl, carboxybutyl, carboxyisobutyl, carboxybutyl, carboxyamyl, carboxyhexyl, carboxyheptyl, carboxyoctyl, carboxyisooctyl, carboxynonyl, carboxydecyl, carboxyundecyl, carboxydodecyl, carboxytetradecyl, carboxyhexadecyl and carboxyoctadecyl, carboxymethyl being preferred.

C₅-C₈cycloalkyl includes cyclopentyl, cyclohexyl and cyclooctyl.

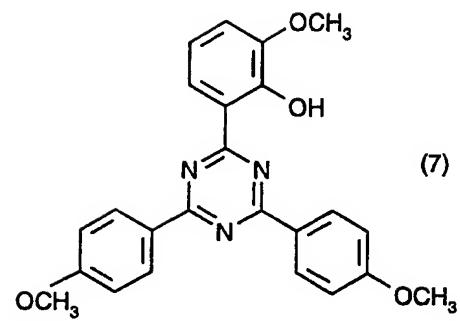
Preferred compounds of formula (1) are those having one of the formulae:



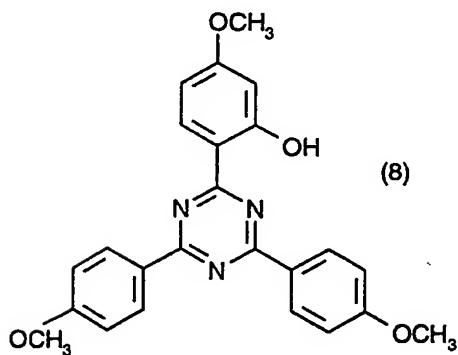
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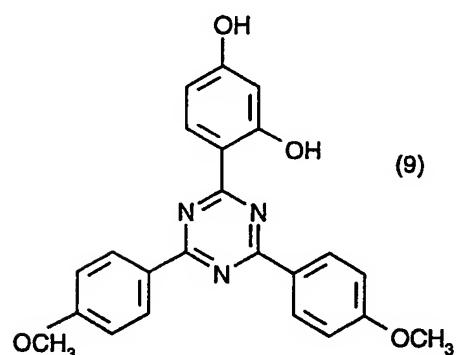
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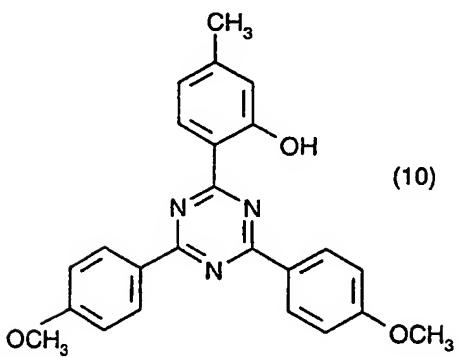
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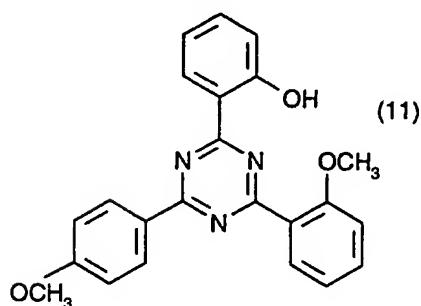
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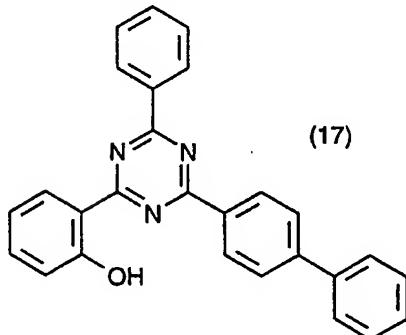
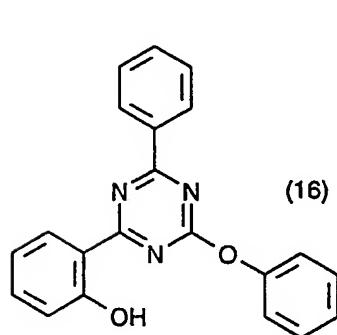
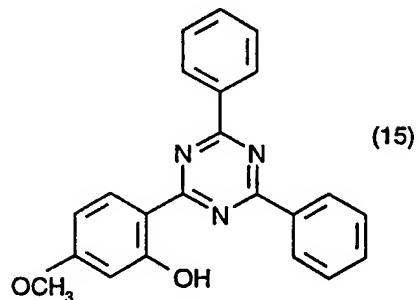
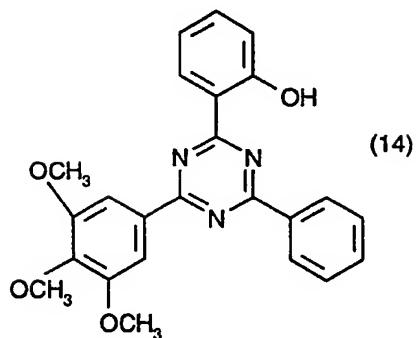
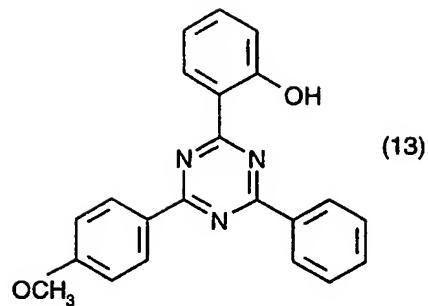
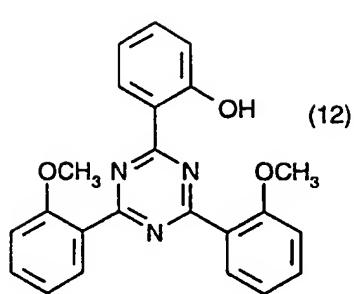


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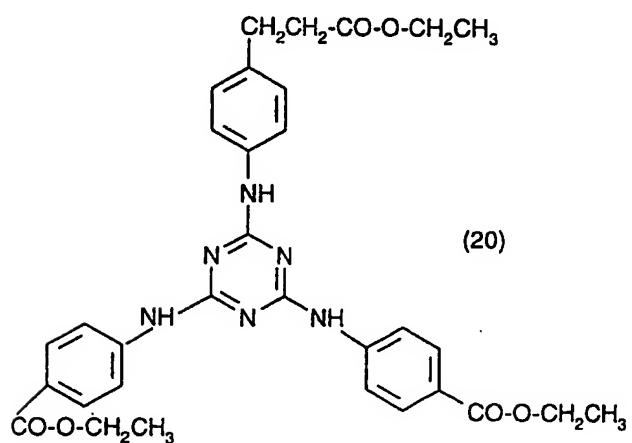
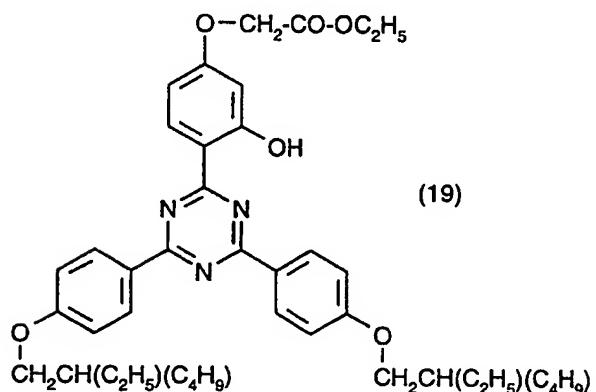
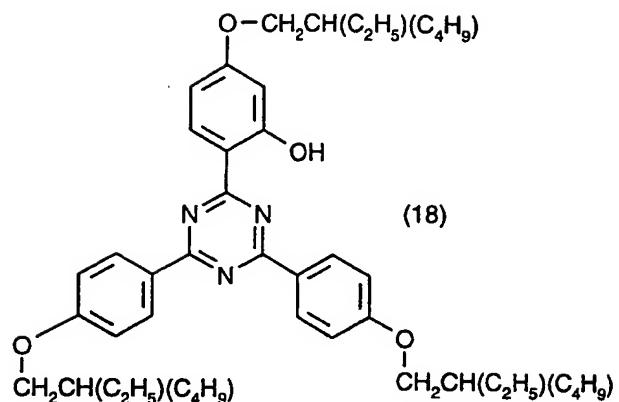


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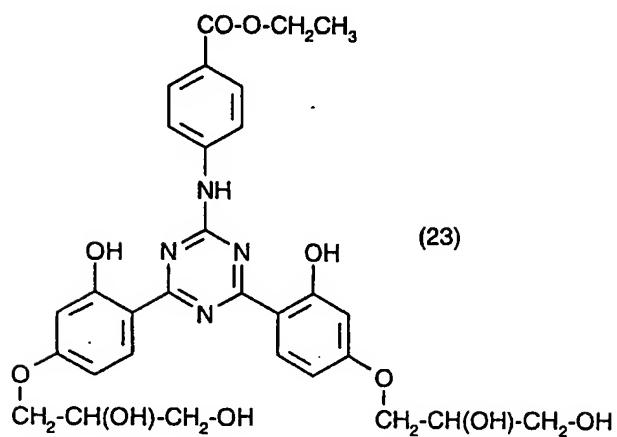
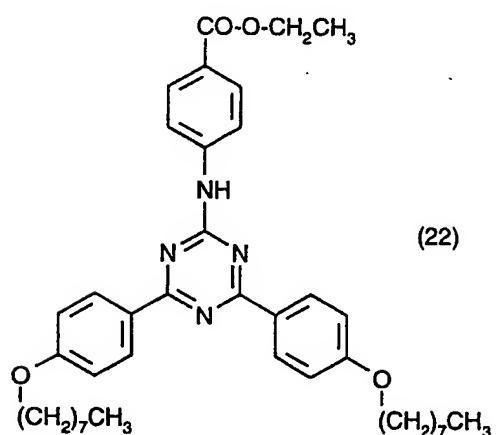
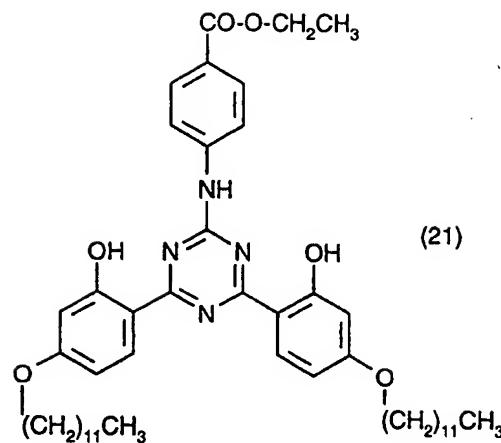
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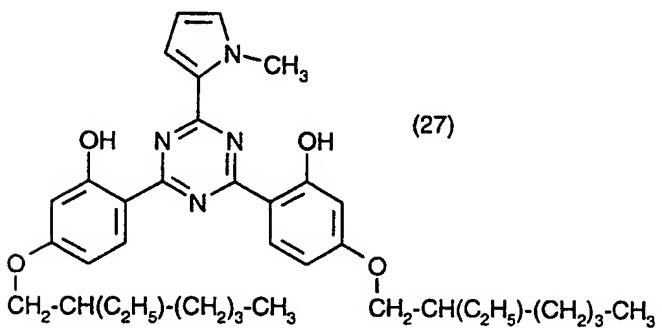
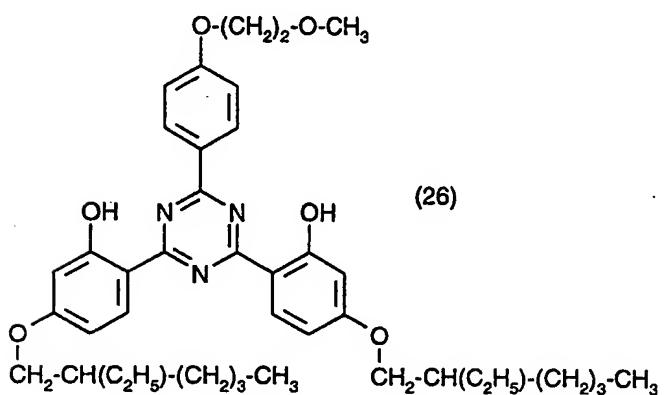
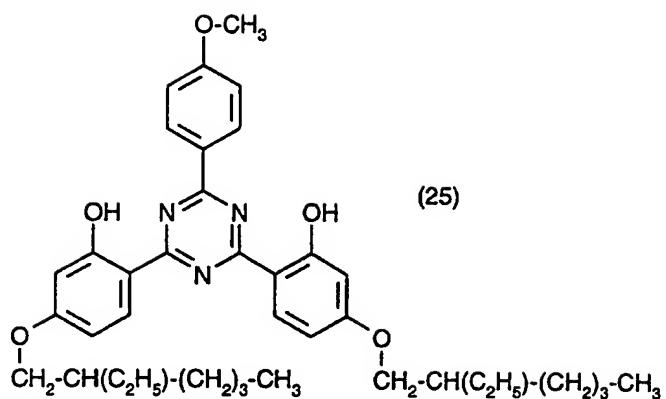
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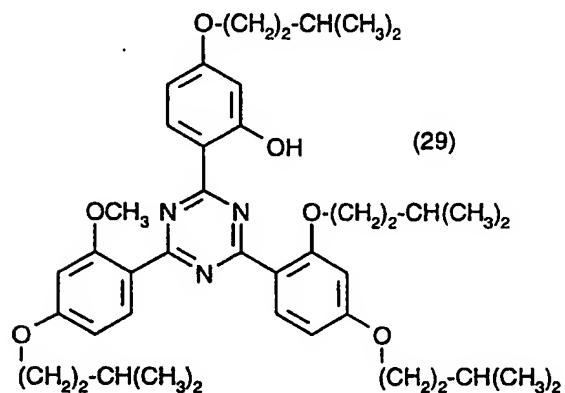
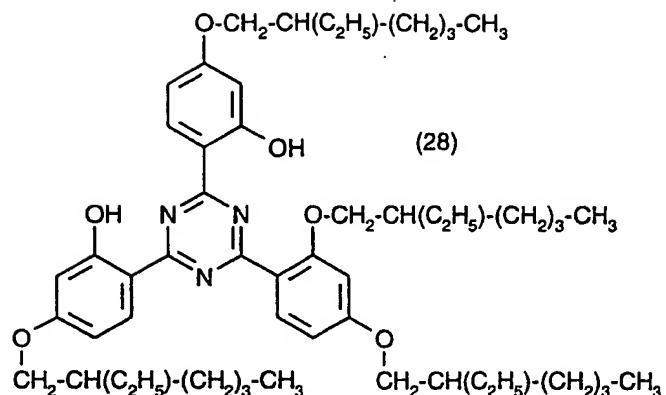
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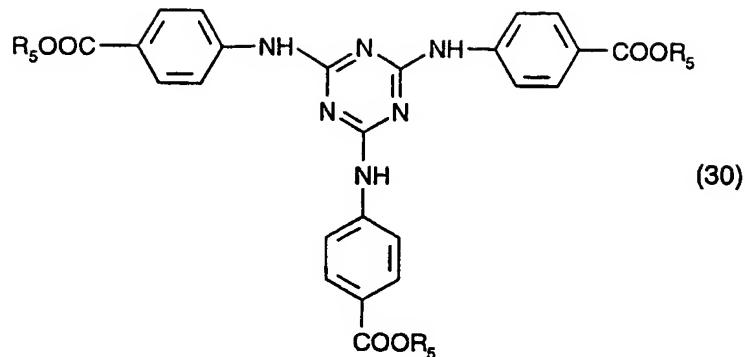
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as well as 2,4,6-tris(diisobutyl-4'-aminobenzalmalonate)-s-triazine and 2,4-bis(diisobutyl-4-aminobenzalmalonate)-6-(4'-aminobenzylidenecamphor)-s-triazine.

Particularly preferred compounds of formula (1) are those having the formula:

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in which the individual radicals R₅ are the same or different and each is hydrogen; an alkali metal; an ammonium group N(R₆)₄ in which R₆ is hydrogen or an organic radical; C₁-C₂₀alkyl; or a polyoxyethylene radical which contains from 1 to 10 ethylene oxide units and the terminal OH group of which may be etherified by a C₁-C₃alcohol.

In relation to the compounds of formula (18), when R₅ is an alkali metal it is preferably potassium or, especially sodium; when R₅ is a group N(R₆)₄ in which R₆ has its previous significance, it is preferably a mono-, di- or tri-C₁-C₄alkylammonium salt, a mono-, di- or tri-C₂-C₄alkanolammonium salt or a C₁-C₂₀alkyl ester thereof; when R₅ is a C₁-C₂₀alkyl group, it is preferably a C₆-C₁₂alkyl group, more preferably a C₈-C₉alkyl group, especially the 3,5,5-trimethylpentyl group or, most particularly, the 2-ethylhexyl group; and when R₅ is polyoxyethylene group, this preferably contains from 2-6 ethylene oxide units.

The compounds of formula (1) are known. The compounds of formula (18) are described, together with their production, in US-A-4617390.

Although they are excellent sun screen agents, the compounds of formula (1) suffer from the drawback that, to date, it has not proved possible to devise satisfactory formulations of them for human sun screen applications.

The compounds of formula (1) are slightly soluble (maximum solubility 13% by weight) in commercial cosmetic oil solvents. After a relatively short time, however, the compounds of formula (1) crystallise out from the said solutions, and thereby lose their sunscreen protective function.

Surprisingly, it has now been found that the compounds of formula (1) are soluble up to levels of 30% by weight in specific types of cosmetic oil solvent, namely i) an alkyl ester of a (hydroxy)polycarboxylic acid; ii) a butylether; iii) an ester of a butyl ether; iv) an alcohol; v) a Guerbet alcohol; or vi) a di(C₁-C₄alkyl)amide of an arylcarboxylic acid. Moreover, such solutions remain stable for at least 3 months with no crystallisation of the compounds of formula (1), even when the solutions are seeded with crystals of the compounds of formula (1).

These new solutions are valuable for the preparation of storage-stable oil-in-water nanoemulsions of compounds of formula (1).

Accordingly, the present invention provides, as a first aspect, a solution, which is especially suitable for use in pharmaceutical or cosmetic applications, comprising a) 1-40%, preferably 10-30% by weight of a compound of formula (1); dissolved in b) a solvent selected from i) a C₁-C₈alkyl ester of a (hydroxy)polycarboxylic acid, with the exclusion of dioctyl malate; ii) a butylether; iii) an ester of a butyl ether; iv) an alcohol; v) a Guerbet alcohol; and vi) a di-(C₁-C₄alkyl)amide of an arylcarboxylic acid.

Component bi) of the solution according to the present invention may be a C₁-C₈alkyl ester formed from a hydroxy group present in the (hydroxy)polycarboxylic acid, from a carboxy group in the (hydroxy)polycarboxylic acid or from both a hydroxy group and a carboxy group.

Component bi) of the solution according to the present invention may be a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, n-amyl, n-hexyl, n-heptyl, n-octyl and isoocetyl ester of pyromellitic, tartaric, lactic and citric acids, or a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, n-amyl, n-hexyl or n-heptyl ester of malic acid. Preferably, however, component bi) of the composition according to the present invention is an ester of citric acid, such as triethyl citrate, acetyl triethyl citrate, acetyl tri-n-butyl citrate, acetyl tri-n-hexyl citrate, n-butyryl tri-n-hexyl citrate, especially tri-butyl citrate.

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Component bii) of the solution according to the present invention is a butylether, especially ethylene glycol butyl ether, diethylene glycol butyl ether, propylene glycol t-butyl ether, methyl-t-butyl ether, a polypropylene glycol of low molecular weight or a (polypropylene glycol)₃₋₅₃ butyl ether.

Component biil) of the solution according to the present invention is an ester of a butyl ether, preferably diethylene glycol butyl ether acetate or propylene glycol methyl ether acetate.

Component biv) of the solution according to the present invention is an alcohol, preferably 3,5,5-trimethylhexanol, 2-butoxyethanol, 2-phenoxyethanol or 2-ethyl-1,3-hexanediol (which has additional insect-repellant activity).

Component bv) of the solution according to the present invention is a Guerbet alcohol, preferably 2-butyloctanol, 2-butyldecanol, 2-hexyloctanol, 2-hexyldecanol, 2-hexyldodecanol, 2-octyldodecanol or 2-decyldodecanol.

Component bvi) of the solution according to the present invention is a di-(C₁-C₄alkyl)amide of an arylcarboxylic acid, especially N,N-diethyl-m-toluamide (which has additional insect-repellant activity).

As a second aspect, the present invention provides a composition comprising emulsified nanoparticles of the solution according to the first aspect of the present invention.

Preferably, the emulsified nanoparticles of the solution according to the first aspect of the present invention have a mean particle size in the range of from 0.01 to 1, more preferably from 0.02 to 0.5, especially from 0.05 to 0.2μ.

The composition according to the second aspect of the present invention may be produced by emulsifying the solution according to the first aspect of the present invention so as to produce nanoparticles of the said solution. The emulsification is conveniently conducted using high pressure homogenisation, e.g. in a microfluidizer.

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The emulsifier used is preferably one which has an HLB value of from 6 to 12. Examples of such emulsifiers are described, for example, in "Cosmetic Bench Reference 1994", published by Allured Publishing Corporation, Carol Stream, USA. Particularly preferred emulsifiers include silicone polyols, fatty acid esters or polyethyleneglycol condensates of sugar alcohols, such as sorbitan monooleate or polyethylene glycol sorbitan monooleate, as well as an alkyl polyglucoside having the formula $C_mH_{2m+1}(C_6H_{10}O_5)_xH$ in which m is an integer ranging from 8 to 16 and x is the mean level of polymerisation of the glucoside moiety ($C_6H_{10}O_5$) and ranges from 1.4 to 1.6. It is particularly preferred to use mixtures of such emulsifiers.

Other useful emulsifiers include phospholipids, which may be of natural or synthetic origin. Naturally occurring phospholipids include phosphatidyl cholines, phosphatidyl serines, phosphatidyl inositol, phosphatidyl ethanolamines, diphosphatidyl glycerols and sphingomyelins which are obtainable from such natural sources as mammalian liver tissue, egg yolk, soybean etc. Synthetic phospholipids may be produced from natural oils such as rapeseed oil. The oil may be hydrogenated, selectively esterified and phosphorylated to form either specific phosphatidates or mixtures of these.

The active ingredient compound of formula (1) may be used together with one or more further UV absorbers which are conventionally used in cosmetic compositions for the protection of human skin against UV radiation.

As already indicated, the composition of the present invention is particularly suitable for use in a sunscreen formulation.

Accordingly, the present invention also provides a sunscreen composition comprising a) 0.1 to 15%, preferably 0.5 to 10% by weight, each based on the final formulation, of a composition according to the second aspect of the present invention; and optionally b) a cosmetically acceptable carrier.

The sunscreen composition of the present invention may be produced by emulsifying the solution according to the first aspect of the present invention, or a composition according to the second aspect of the present invention, and any optional carrier components, according to known methods. Preferably, the emulsification is conducted using a high pressure

homogenizer, conveniently at a pressure of 500-1500, especially 1000-1500 atmospheres. The nanoemulsions so obtained may then be formulated with further components which are known to perform a useful function in a sunscreen composition. Examples of such further components include, e.g., emollients, skin moisturisers, skin tanning accelerators, antioxidants, emulsion stabilisers, thickening agents such as xanthan gum, moisture-retention agents such as glycerine, film formers, preservatives, perfumes and colourants.

The sunscreen composition of the invention may be formulated as a water-in oil or an oil-in-water emulsion, an oil or oil-alcohol lotion, a vesicular dispersion of an ionic or nonionic amphiphilic lipid, a gel, a solid stick or an aerosol formulation.

When formulated as a water-in oil or an oil-in-water emulsion, the cosmetically acceptable carrier preferably comprises 5 to 50% of an oil phase, 5 to 20% of an emulsifier and 30 to 90% of water, each by weight based on the total weight of the carrier.

The oil phase may comprise, in addition to the solvent, component b), any oil conventionally used in cosmetic formulations, e.g., one or more of a hydrocarbon oil, a wax, a natural oil, a silicone oil, a fatty acid ester or a fatty alcohol. Preferred mono- or polyols are ethanol, isopropanol, propylene glycol, hexylene glycol, glycerine and sorbitol.

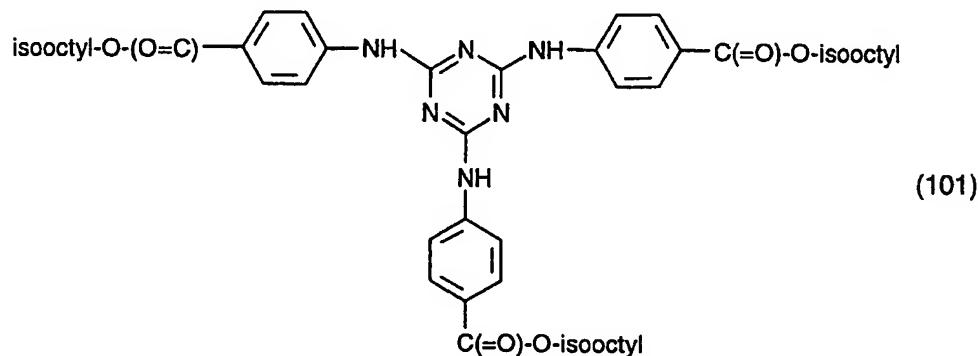
The emulsifier also may comprise any emulsifier conventionally used in cosmetic formulations, e.g., one or more of an ethoxylated ester of a natural oil derivative such as a polyethoxylated ester of hydrogenated castor oil; a silicone oil emulsifier such as a silicone polyol; an optionally ethoxylated fatty acid soap; an ethoxylated fatty alcohol; an optionally ethoxylated sorbitan ester; an ethoxylated fatty acid; an ethoxylated glyceride; or an alkyl polyglucoside having the formula $C_mH_{2m+1}(C_6H_{10}O_5)_xH$ in which m and x have their previous significance.

The sunscreen composition of the invention provides excellent protection of the human skin against the damaging effects of sunlight, while permitting safe tanning of the skin. Moreover, the sunscreen composition of the invention has a skin waterproofing effect and may, depending on the solvent used, exert an insect-repellant action.

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The following Examples further illustrate the present invention. Parts shown therein are parts by weight unless otherwise stated.

Example 1: 50g of 2,4,6-trianilino-p-(carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine having the formula:



is dissolved in 150g of tributyl citrate at 60°C., with stirring. A clear solution is obtained.

As a test of its storage stability, the solution, cooled to 25°C., is seeded with crystals of 2,4,6-trianilino-p-(carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine. Even after three months storage, the solution remains clear without any trace of crystallisation.

Example 2: The solution obtained in Example 1 is converted, by known methods, into an oil-in-water sun screen nanoemulsion having the following composition:

Solution of Example 1	40 parts
PEG-20-sorbitan monooleate	2.5 parts
Sorbitan monooleate	7.5 parts
Water	50 parts

Example 3: The solution obtained in Example 1 is converted, by known methods, into an oil-in-water sun screen nanoemulsion having the following composition:

Solution of Example 1	40 parts
PEG-20-sorbitan monooleate	2.5 parts
Sorbitan monooleate	7.5 parts
Polydimethylsiloxane-copolyol	2 parts
Water	48 parts

Example 4: A nanoemulsion is produced having the following composition:

Tributyl citrate	300 parts
Compound of formula (101)	100 parts
Sorbitan monooleate	75 parts
PEG-20-sorbitan monooleate	25 parts
Water	500 parts

300 Parts of tributyl citrate are placed in a glass container and heated to 60-80°C. 100 Parts of the compound of formula (101) are then added, with stirring, to give a clear solution. 75 Parts of sorbitan monooleate and 25 parts of PEG-20-sorbitan monooleate are added and the whole is stirred until a clear solution is obtained.

Under intensive stirring (600-800 rpm using a blade stirrer), 500 parts of water are slowly added. A milky water-in-oil emulsion results, the mean particle size of which is about 20 μ . This emulsion is storage stable for only a short time. Part of this emulsion is homogenised twice at 1000 bar pressure using a high pressure emulsifying machine. This additional treatment provides a nanoemulsion having a mean particle size of about 400 nm and a storage stability of at least 9 months.

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Example 5: A nanoemulsion is produced having the following composition:

Tributyl citrate	45 parts
Compound of formula (101)	15 parts
Phospholipid (Phospholipon 80)	20 parts
Ethanol	80 parts
Water	340 parts

Using the procedure described in Example 4, 15 parts of the compound of formula (101) are dissolved in 45 parts of tributyl citrate in a first glass container at 60-80°C. and the whole is then cooled to give a clear solution (mixture A).

In a separate glass container, 20 parts of phospholipid (Phospholipon 80) are dissolved in 80 parts of ethanol at 25°C. and this solution is added to mixture A to produce a clear solution (mixture B).

Mixture B is placed in the first vessel of an emulsification machine (Minisonic®) and 340 parts of water are placed in the second vessel. The water is then mixed with mixture B at a pressure of about 12 bar using ultra-sound. The mixture so obtained is homogenised for 5 minutes with the Minisonic machine, again at about 12 bar. During the homogenisation process, the temperature of the mixture rises to 60°C. The whole is then stirred cold, giving an emulsion having a mean particle size of about 780 nm.

Part of this emulsion is homogenised twice at 1000 bar pressure using a high pressure emulsifying machine. This additional treatment provides a nanoemulsion having a mean particle size of about 400 nm and a storage stability of at least 5 months.

Example 6: A nanoemulsion is produced having the following composition:

Tributyl citrate	45 parts
Compound of formula (101)	15 parts
Phospholipid (Phospholipon 80)	20 parts
Glycerine	80 parts
Water	340 parts

Using the procedure described in Example 5, after the homogenisation with the Minisonic machine, an emulsion is obtained having a mean particle size of about 1000 nm.

Part of this emulsion is homogenised twice at 1000 bar pressure using a high pressure emulsifying machine. This additional treatment provides a nanoemulsion having a mean particle size of about 700 nm and a storage stability of at least 5 months.

Example 7: A nanoemulsion is produced having the following composition:

N,N-Diethyl-m-toluamide	300 parts
Compound of formula (101)	100 parts
Sorbitan monooleate	150 parts
PEG-20-sorbitan monooleate	50 parts
Water	400 parts

The nanoemulsion is produced using the procedure described in Example 4.

The in-vitro Sun Protection Factor (SPF) is determined by measurement of the UV light transmitted through the nanoemulsion, using a double grating spectrophotometer fitted with an Ulbricht bowl. Calculation of SPF is conducted as described by B.L.Difley and J.Robson in J. Soc. Cosm. Chem. 40 (1989), pp. 130-131. The SPF rating obtained is 8.9.

In addition to its excellent SPF rating, the nanoemulsion also exhibits insect-repellant activity.

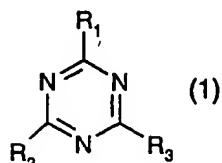
Examples 8 to 10:

Using the procedure described in Example 4, but replacing the tributyl acetate component by butyl lactate, dioctyl adipate or dioctyl succinate, respectively, a nanoemulsion having properties similar to that of Example 4 is obtained.

Similar results are obtained when, in the Examples 1 to 10, the compound of formula (101) is replaced by a different compound of formula (1), such as a compound of formula (2) to (17); and/or the solvent component, e.g. tributyl citrate, is replaced by a butyl ether such as ethylene glycol butyl ether, diethylene glycol butyl ether, propylene glycol t-butyl ether, methyl-t-butyl ether, a polypropylene glycol of low molecular weight or a (polypropylene glycol)₃₋₅₃ butyl ether; an ester of a butyl ether such as diethylene glycol butyl ether acetate or propylene glycol methyl ether acetate; an alcohol such as 3,5,5-trimethylhexanol, 2-butoxyethanol, 2-phenoxyethanol or 2-ethyl-1,3-hexanediol (which has additional insect-repellant activity); or a Guerbet alcohol such as 2-butyloctanol, 2-butyldecanol, 2-hexyloctanol, 2-hexyldecanol, 2-hexylundecanol, 2-octylundecanol or 2-decyldodecanol.

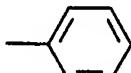
Claims

1. A solution comprising a) 1-40% by weight of a triazine compound having the formula:



in which R₁, R₂ and R₃, independently, are H, OH, C₁-C₁₈alkoxy, NH₂, NH-R₄ or N(R₄)₂ in which R₄ is C₁-C₁₈alkyl, OR₄ in which R₄ has its previous significance, phenyl, phenoxy or anilino, or pyrrolo in which the respective phenyl or pyrrolo moieties are optionally substituted by one, two or three substituents selected from OH, carboxy, C₁-C₁₈alkyl or -alkoxy, C₁-C₁₈carboxyalkyl, C₅-C₈cycloalkyl, a methylidene camphor group, a group

-(CH=CH)_nC(=O)-OR₄ in which n is 0 or 1 and R₄ has its previous significance or a

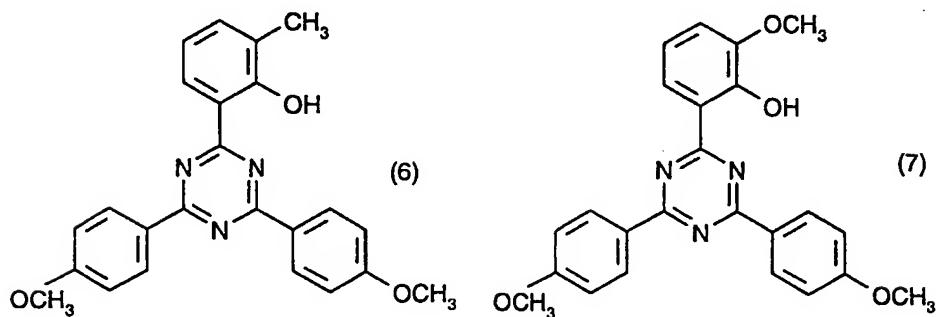
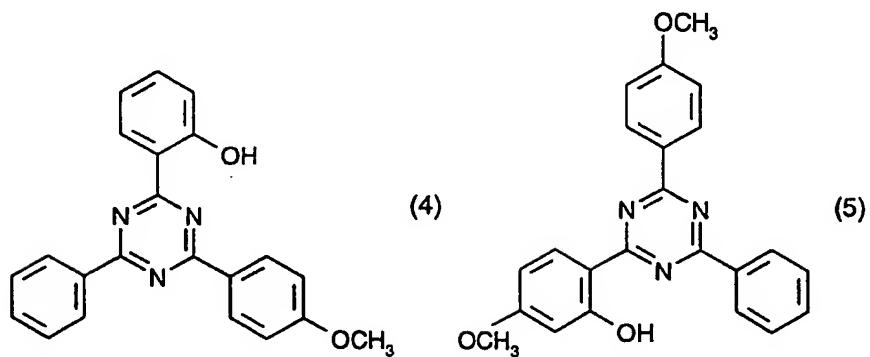
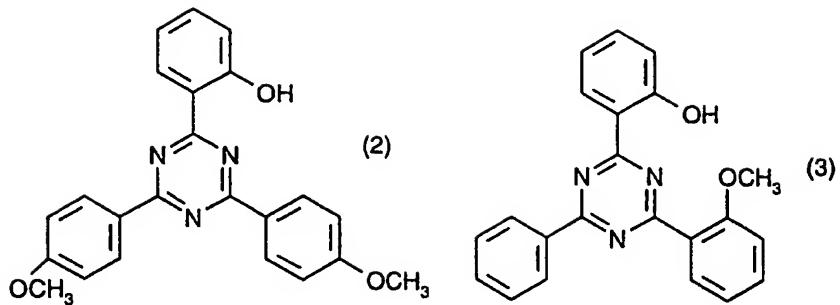
group -CH=CH-C(=O)-OH or the corresponding alkali metal,

ammonium, mono-, di- or tri-C₁-C₄alkylammonium, mono-, di- or tri-C₂-C₄alkanolammonium salts, or the C₁-C₁₈alkyl esters thereof; dissolved in b) a solvent selected from i) a C₁-C₈alkyl ester of a (hydroxy)polycarboxylic acid, with the exclusion of dioctyl malate; ii) a butylether; iii) an ester of a butyl ether; iv) an alcohol; v) a Guerbet alcohol; and vi) a di-(C₁-C₄alkyl)amide of an arylcarboxylic acid.

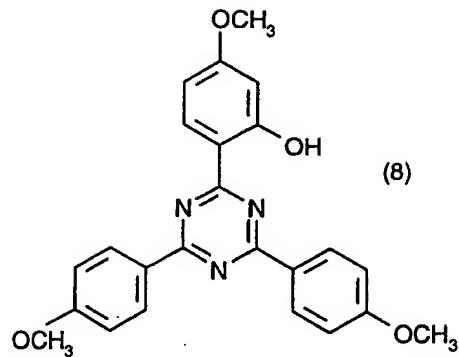
2. A solution according to claim 1 which comprises 10-30% by weight of a compound having the formula (1).

3. A solution according to claim 1 or 2 in which the compound of formula (1) has one of the formulae:

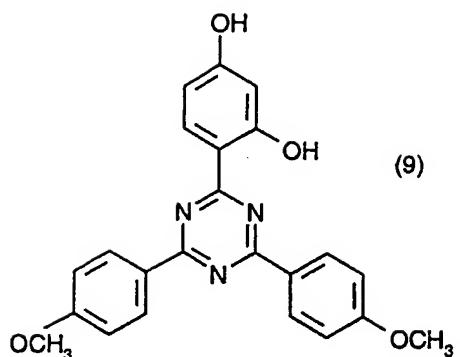
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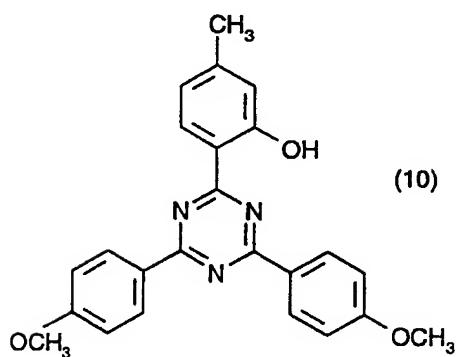
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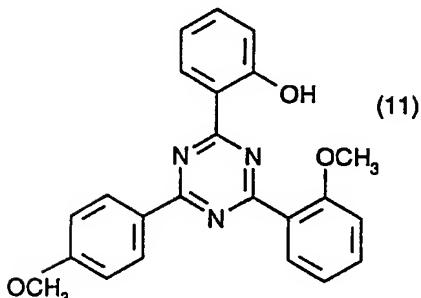
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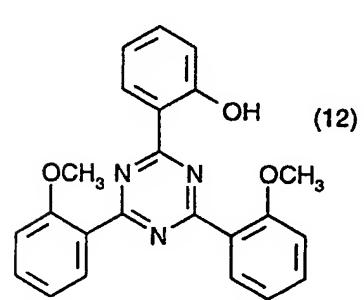
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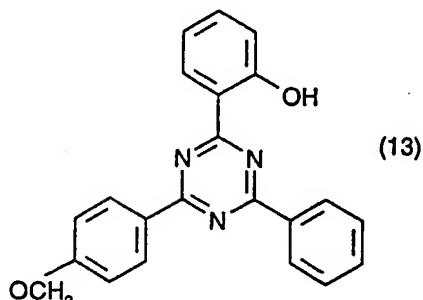
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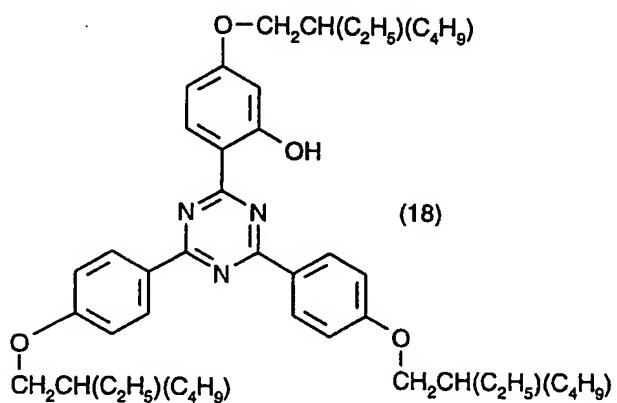
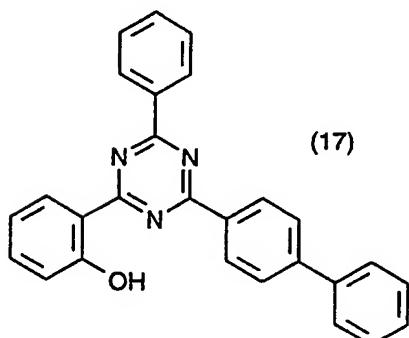
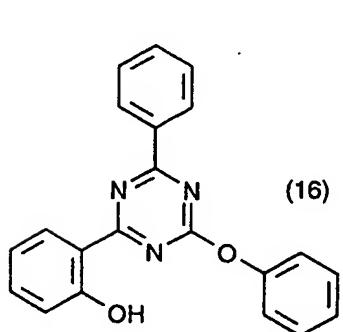
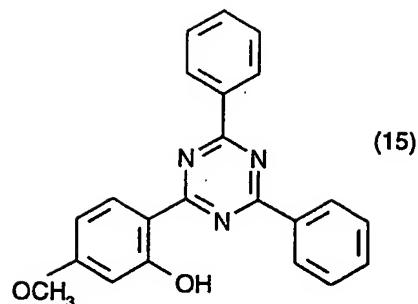
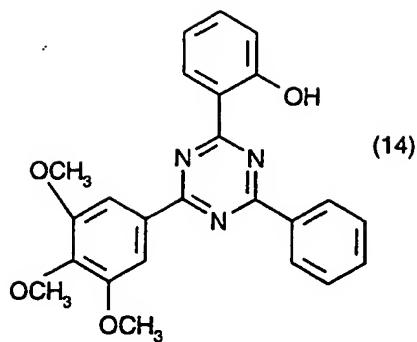


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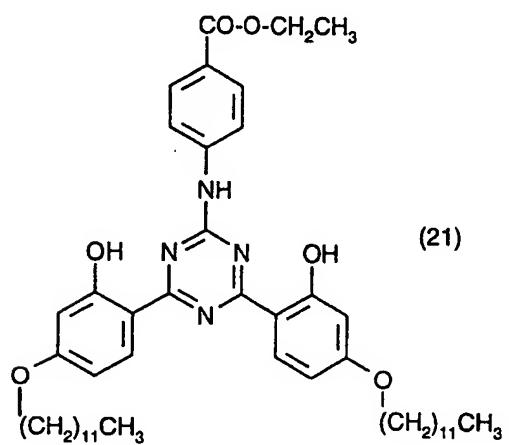
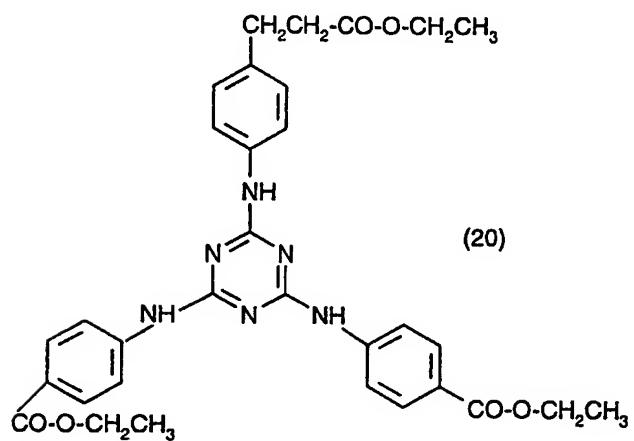
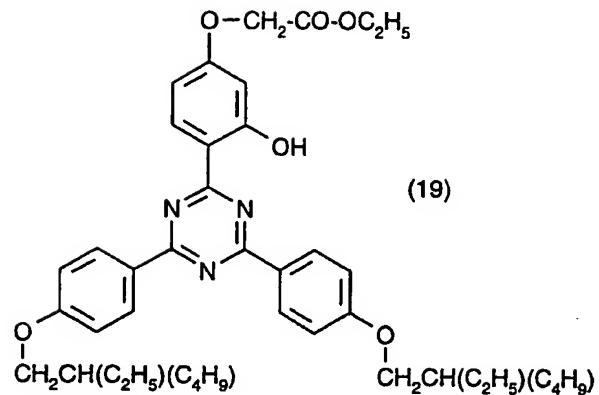


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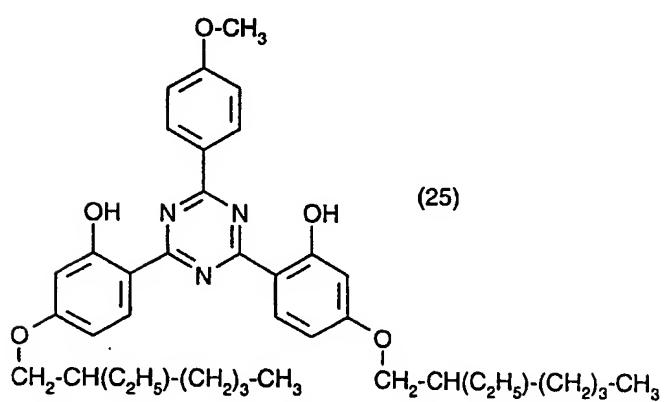
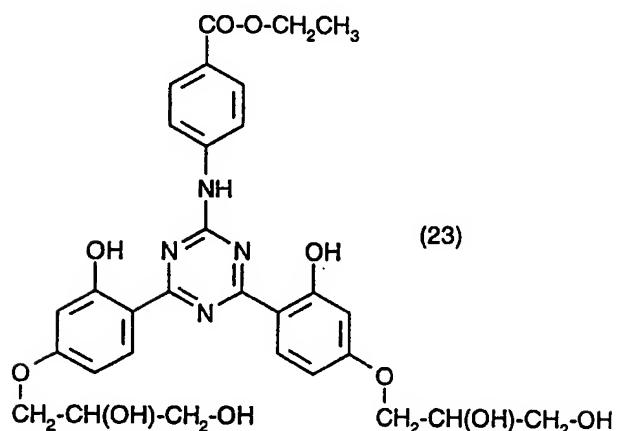
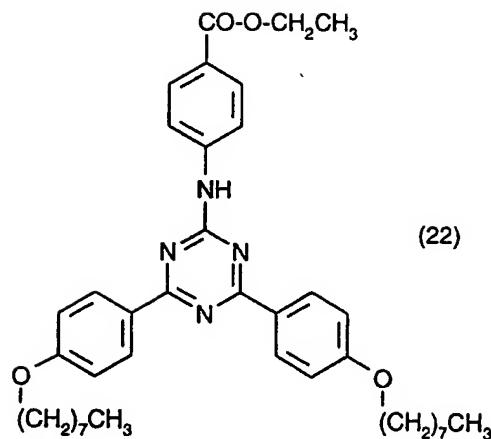
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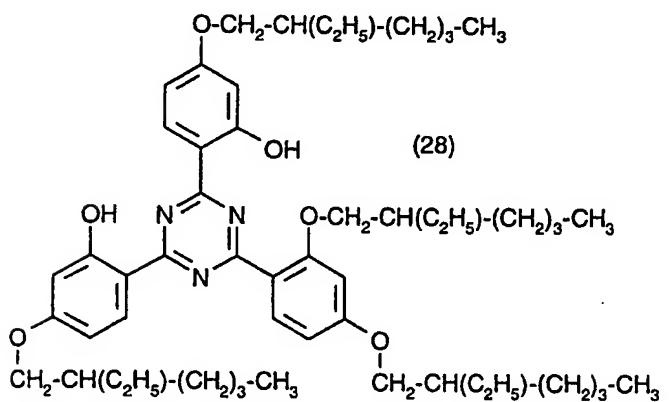
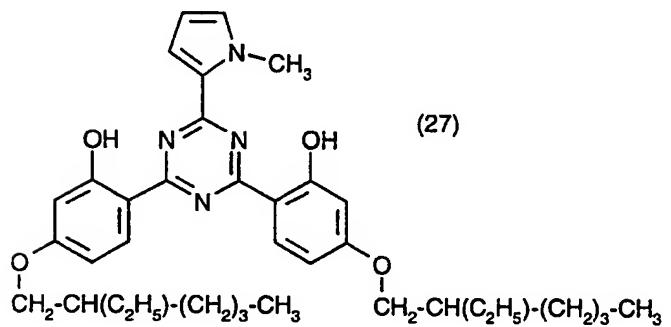
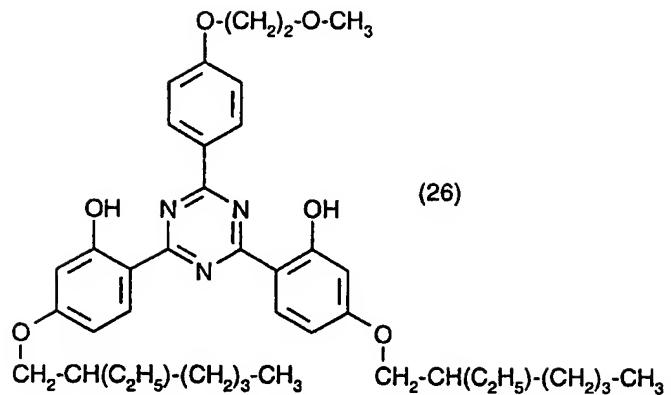
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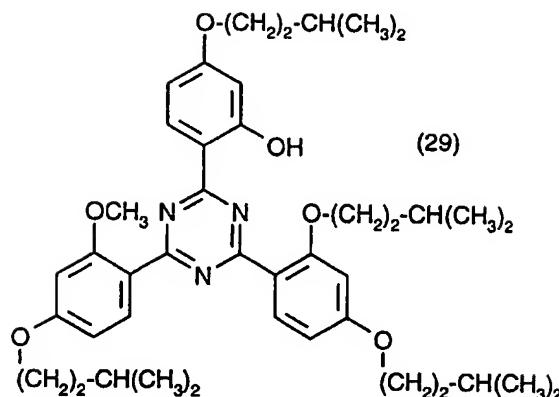
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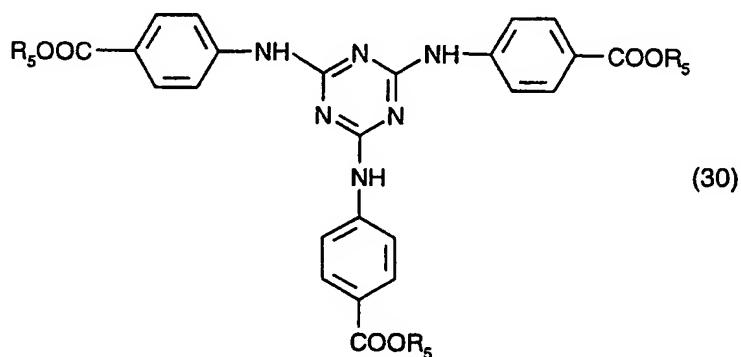


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or is 2,4,6-tris(diisobutyl-4'-aminobenzalmalonate)-s-triazine or
2,4-bis(diisobutyl-4-amino-benzalmalonate)-6-(4'-aminobenzylidenecamphor)-s-triazine.

4. A solution according to claim 1 in which the compound of formula (1) has the formula:



in which the individual radicals R₅ are the same or different and each is hydrogen; an alkali metal; an ammonium group N(R₆)₄ in which R₆ is hydrogen or an organic radical; C₁-C₂₀alkyl; or a polyoxyethylene radical which contains from 1 to 10 ethylene oxide units and the terminal OH group of which may be etherified by a C₁-C₃alcohol.

5. A solution according to claim 4 in which when R₅ is an alkali metal it is potassium or sodium; when R₅ is a group N(R₆)₄ in which R₆ is as defined in claim 4, it is a mono-, di- or tri-C₁-C₄alkylammonium salt, a mono-, di- or tri-C₂-C₄alkanolammonium salt or a C₁-C₂₀alkyl ester thereof; when R₅ is a C₁-C₂₀alkyl group it is a C₆-C₁₂alkyl group; and when R₅ is polyoxyethylene group, this contains from 2-6 ethylene oxide units.

6. A solution according to any of the preceding claims in which component bi) is a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, n-amyl, n-hexyl, n-heptyl, n-octyl or isoocetyl ester of pyromellitic, tartaric, lactic or citric acid or is a methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert.-butyl, n-amyl, n-hexyl or n-heptyl ester of malic acid.
7. A solution according to claim 6 in which component bi) is triethyl citrate, acetyl triethyl citrate, acetyl tri-n-butyl citrate, acetyl tri-n-hexyl citrate, n-butyryl tri-n-hexyl citrate or tri-butyl citrate.
8. A solution according to claim 6 in which component bi) is tri-butyl citrate.
9. A solution according to any of claims 1 to 5 in which component bii) is ethylene glycol butyl ether, diethylene glycol butyl ether, propylene glycol t-butyl ether, methyl-t-butyl ether, a polypropylene glycol of low molecular weight or a (polypropylene glycol)₃₋₅₃ butyl ether.
10. A solution according to any of claims 1 to 5 in which component biii) is diethylene glycol butyl ether acetate or propylene glycol methyl ether acetate.
11. A solution according to any of claims 1 to 5 in which component biv) is 3,5,5-trimethylhexanol, 2-butoxyethanol, 2-phenoxyethanol or 2-ethyl-1,3-hexanediol.
12. A solution according to any of claims 1 to 5 in which component bv) is 2-butyloctanol, 2-butydecanol, 2-hexyloctanol, 2-hexyldecanol, 2-hexylidodecanol, 2-octylidodecanol or 2-decyltetraacanol.
13. A solution according to any of claims 1 to 5 in which component bvi) is N,N-diethyl-m-toluamide.
14. A composition comprising emulsified nanoparticles of a solution as claimed in any of the preceding claims.
15. A composition according to claim 14 in which the emulsified nanoparticles have a mean particle size in the range of from 0.01 to 1.0 μ .

16. A composition according to claim 15 in which the emulsified nanoparticles have a mean particle size in the range of from 0.02 to 0.5 μ .
17. A composition according to claim 16 in which emulsified nanoparticles have a mean particle size in the range of from 0.05 to 0.2 μ .
18. A composition according to any of claims 14 to 17 in which the composition has been produced by emulsifying a solution claimed in any of claims 1 to 13 so as to produce nanoparticles of the said solution.
19. A composition according to claim 18 in which the emulsification is conducted using high pressure homogenisation using a microfluidiser.
20. A composition according to claim 18 or 19 in which the emulsification is conducted using an emulsifier which has an HLB value of from 6 to 12.
21. A composition according to claim 20 in which the emulsifier is a silicone polyol, a fatty acid ester or polyethyleneglycol condensate of a sugar alcohol or an alkyl polyglucoside having the formula $C_mH_{2m+1}O(C_6H_{10}O_5)_xH$ in which m is an integer ranging from 8 to 16 and x is the mean level of polymerisation of the glucoside moiety ($C_6H_{10}O_5$) and ranges from 1.4 to 1.6.
22. A composition according to claim 21 in which the emulsifier is sorbitan monooleate or polyethylene glycol sorbitan monooleate.
23. A composition according to any of claims 20 to 22 in which the emulsifier is a phospholipid.
24. A composition according to claim 23 in which the phospholipid is one or more of a phosphatidyl choline, phosphatidyl serine, phosphatidyl inositol, phosphatidyl ethanolamine, diphosphatidyl glycerol or a sphingomyelin.

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25. A composition according to any of claims 20 to 24 in which a mixture of emulsifiers is used.
26. A sunscreen composition comprising a) 0.1 to 15% by weight, based on the final formulation, of a composition according to any of claims 14 to 25; and, optionally, b) a cosmetically acceptable carrier.
27. A sunscreen composition according to claim 26 comprising a) 0.5 to 10% by weight, based on the final formulation, of a composition according to any of claims 14 to 25; and, optionally, b) a cosmetically acceptable carrier.
28. A sunscreen composition according to claim 26 or 27 which has been produced by emulsifying a solution according to any of claims 1 to 13.
29. A sunscreen composition according to claim 28 which has been produced by conducting the emulsification at a pressure of 500-1500 atmospheres.
30. A sunscreen composition according to claim 29 which has been produced by conducting the emulsification at a pressure of 1000-1500 atmospheres.
31. A sunscreen composition according to any of claims 28 to 30 which is then formulated with further components selected from emollients, skin moisturisers, skin tanning accelerators, antioxidants, emulsion stabilisers, thickening agents, moisture retention agents, film formers, preservatives, perfumes and colourants.
32. A sunscreen composition according to any of claims 26 to 31 in which the solution according to any of claims 1 to 13 is used together with one or more UV absorbers which are conventionally used in cosmetic compositions for the protection of human skin against UV radiation.
33. A sunscreen composition according to any of claims 26 to 32 which is formulated as a water-in oil or an oil-in-water emulsion, an oil or oil-alcohol lotion, a vesicular dispersion of an ionic or nonionic amphiphilic lipid, an oil-alcohol or alcohol gel, a solid stick or an aerosol formulation.

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34. A sunscreen composition according to claim 33 which is formulated as a water-in oil or an oil-in-water emulsion and component b) comprises 5 to 50% of an oil phase, 5 to 20% of an emulsifier and 30 to 90% of water, each by weight based on the total weight of the carrier.
35. A sunscreen composition according to claim 34 in which the oil phase comprises one or more of a hydrocarbon oil, a wax, a natural oil, a silicone oil, a fatty acid ester or a fatty alcohol.
36. A sunscreen composition according to claim 34 or 35 in which the emulsifier comprises one or more of an ethoxylated ester of a natural oil derivative; a silicone polyol emulsifier; an optionally ethoxylated fatty acid soap; an ethoxylated fatty alcohol; an optionally ethoxylated sorbitan ester; an ethoxylated fatty acid; an ethoxylated glyceride; or an alkyl polyglucoside having the formula $C_mH_{2m+1}(C_6H_{10}O_5)_xH$ in which m and x are as defined in claim 21.
37. A sunscreen composition according to claim 36 in which the ethoxylated ester of a natural oil derivative is a polyethoxylated ester of hydrogenated castor oil; and the silicone oil emulsifier is silicone polyol.
38. A method of producing a storage stable nanoemulsion according to any of claims 14 to 25, comprising emulsifying a solution according to any of claims 1 to 13.
39. A method according to claim 38 in which the emulsification is conducted using high pressure homogenisation.
40. A method of producing a sunscreen composition according to any of claims 26 to 37, comprising emulsifying a solution according to any of claims 1 to 8 or a composition according to any of claims 9 to 20 and any optional carrier component.
41. A method according to claim 40 in which the emulsification is conducted using a high pressure homogeniser.

42. A method according to claim 40 or 41 in which the emulsification is conducted at 500 to 1500 atmospheres.

INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/EP 96/03043

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP,A,0 685 226 (OREAL) 6 December 1995 see page 2-3 see page 4, line 45-58 see table 1 see claims 1-4,7,8,18-20 ---	1-5
X	EP,A,0 457 687 (OREAL) 21 November 1991 see page 2, line 43-44 see page 3, line 32-33 see page 4, line 5-7 see page 4, line 27-29 see examples A,B,C see claims 1-3,7,13 ---	1-5

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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- *E* earlier document but published on or after the international filing date
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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search 18 December 1996	Date of mailing of the international search report 7.01.97
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Authorized officer

Sierra Gonzalez, M

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 96/03043

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 087 098 (BASF AG) 31 August 1983 cited in the application see page 7, line 13-16 see examples 9,10 see claims 1-3,5 ---	1-5
X,P	EP,A,0 689 828 (OREAL) 3 January 1996 see the whole document ---	1-5
P,A	EP,A,0 685 223 (OREAL) 6 December 1995 see the whole document -----	1-41

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat'l Application No

PCT/EP 96/03043

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